UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,663	06/25/2003	Pierre Charneau	03495.0199-01	8007

22852 7590 02/26/2008

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
02/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/602,663	CHARNEAU ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-46,50,51 and 62-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-46,50,51 and 62-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed 30 November 2007. Claims 1-40, 47-49 and 52-61 have been cancelled. Claims 62-77 have been added. Claims 41-46, 50, 51 and 62-77 are pending and currently examined.

Double Patenting

The Examiner notes with appreciation that Applicants have filed a terminal disclaimer. The nonstatutory double patenting rejection of claims 41-51 as being unpatentable over claims 1-4, 8-11, 14, 15, 22 and 23 of US Patent No. 6,682,907 is **withdrawn**. Likewise, the provisional nonstatutory double patenting rejection of 41-45 and 51 as being unpatentable over claims 36, 40, 43, 44 and 69 of copending Application No. 10/313,038 is **withdrawn**.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

New rejection necessitated by amendment: Claims 62-65 and 74-77 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claims 62 and 74 both recite the limitation "comprising the vector … in a protein envelope" that is confusing because it can be read in two ways: Is the vector

inside a protein envelope of the non-infectious particle or is the transgenic protein expressed from the vector in a protein envelope of the particle? Thus, all the dependent claims are also rejected.

Comment [BC1]: I don't see why it is indefinite - they don't claim it's a viral particel, just a "particle" - so it's their vector in any protein. Now are there enablement problems? Quite possibly - do they explain how to make an "envelope" other than a viral capsid? Probably not. Do they teach how to use any other kind of "particle?" Now claim 63 looks indefinite - are the additional vectors part of the particle? are the gag, pol and env proteins part of the envelope, or are they "provided" some other way?
I don't think there is an enablement problem. I rewrote the explanation of this rejection.
The Gag (viral capsid), Pol (viral polymerase) and Env (viral envelope) proteins form the viral particle, the claim clearly recites they are provided by one or more additional vector(s). These vectors are transformed into cells, the viral proteins are expressed by the cells and packaged into the non-infectious particles.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 41-46, 50 and 51 under 35 U.S.C. §103(a) as being obvious over Verma *et al.* (WO 97/12622) in view of Charneau *et al.* (1994, hereinafter Charnearu'94) and Charneau *et al.* (1992, hereinafter Charneau'92) **is maintained and extended to new claims 62-77**.

Claims 41-46, 50 and 51 are directed to a recombinant, non-replicative, non-infectious, lentiviral transfer vector deprived of functional genes encoding lentiviral Gag, Pol, and Env proteins, comprising: (1) a polynucleotide comprising a cis-acting central polypurine tract ("cPPT"), and a cis-acting central terminator sequence ("CTS"), wherein the cPPT and CTS are of the central polypurine tract ("cPPT") retroviral-like origin and derived from a retrotransposon and which form a triple-stranded sequence (DNA triplex); (2) a defined nucleotide sequence (transgene or sequence of interest); and (3) regulatory signals for reverse transcription, expression, and packaging, wherein said

regulatory signals are of retroviral or retroviral-like origin; and wherein the DNA triplex transfers the defined nucleotide sequence into the nucleus of a cell.

Claims 62-77 recite the additional limitation of a non-infectious particle wherein the HIV Gag, Pol and Env proteins are provided by one or more additional vector(s).

Verma *et al.* disclose a recombinant, non-replicative, non-infectious retroviral transfer vector comprising: (1) a transgene encoding for luciferase or β-galactosidase, and (2) retroviral regulatory signals, HIV-1 LTR and RRE. Verma *et al.* further disclose two additional vectors, a packaging construct comprising HIV Gag, Pol, Vif, Tat, Rev and Nef, and a pseudotyping MLV vector comprising HIV Env. See Figure 1. The Verma retroviral transfer vector does not comprise cPPT and CTS.

Comment [BC2]: What about the protein envelope? Is this in Verma or not?
Yes, the protein envelope is expressed by the third vector, the pseudotyping MLV vector.

Charneau'94 discloses that cPPT is an important *cis*-acting sequence for initiating DNA transcription by priming DNA synthesis. See page 651, the sentence bridging the two columns, and right column, last paragraph. Charneau'94 further discloses a *cis*-acting HIV-1 CTS that is essential for terminating DNA synthesis by displacing the completed DNA strand. See page 652, left column, 2nd paragraph. Charneau'94 specifically discloses the nucleotide sequence of HIV-1 CTS. See page 654, Figure 2. Charneau'94 does not disclose the nucleotide sequence of cPPT.

Charneau'92 discloses the nucleotide sequence of HIV-1 cPPT. See page 2815, Figure 1(a). Charneau'92 also discloses that cPPT is an important sequence for initiating DNA transcription. See page 2814, left column.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the Verma retroviral transfer vector so as to insert the

Deleted: intiation

initiation signal, cPPT, and the termination signal, CTS, as taught by Charneau'92 and Charneau'94, upstream and downstream the coding sequence of the transgene in the retroviral transfer vector taught by Verma *et al.* The skilled artisan would have been motivated to do so to improve the transfer, integration and sustained long-term expression of the transgene inside a cell. There would have been a reasonable expectation of success, given the routine practice of molecular cloning in the art and the importance of cPPT and CTS for the initiation and termination of DNA synthesis, as taught by the two Charneau references. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicants' arguments filed on 30 November 2007 have been fully considered but are not persuasive. Applicants first argue that the Verma transfer vector does not include "regulatory signals for reverse transcription, expression, and packaging." Examiner respectfully disagrees. The Verma transfer vector comprises a transgene, HIV-1 long term repeat (LTR) and Rev response element (RRE). The HIV-1 LTR, which has promoter activity, and the RRE, which helps the splicing of pre-mRNA in post-translational modification during protein synthesis, are the regulatory signals for reverse transcription, expression and packaging.

Applicants also argue that the two Charneau references do not teach the use of cPPT and CTS in a recombinant, non-replicative, non-infectious, lentiviral transfer vector. However, this limitation is taught by Verma *et al.*, which is applied as the

primary reference in this rejection. Verma's transfer vector comprising a transgene and the regulatory signals, HIV-1 LTR and RRE, is deprived of functional genes encoding lentiviral Gag, Pol and Env proteins. HIV viral DNA replication requires reverse transcriptase (RT), which is part of the Pol protein. HIV viral maturation and particle formation requires the Gag protein. Host cell attachment requires the HIV Env protein, Therefore, without the Pol, Gag and Env proteins, the Verma transfer vector is non-infectious and non-replicative. Although the secondary references do not explicitly teach the use of cPPT and CTS in a recombinant, non-replicative, non-infectious, lentiviral transfer vector, the Charneau references disclose their functions in initiating and terminating the process of DNA synthesis, which is a process generally required for any kind of gene expression like the claimed transgene.

Applicants further argue that Examiner's reasoning regarding the motivation of enhanced replication is directed away from the claimed invention. Applicants seemed to have misconstrued Examiner's meaning of the word "replication" here, which is in the context of DNA replication of the transgene in order to express the transgene, *not* in the context of a replicative viral particle or vector.

Additionally, Applicants argue that nothing in the references motivates creation of a vector that combines cPPT and CTS sequences with a vector that is "deprived of functional genes encoding lentiviral Gag, Pol, and Env proteins," as recited by the claims. An explicit suggestion or motivation in the references is not the standard. The suggestion to combine or modify the teaching of the prior art can be established either in the references themselves or in the knowledge generally available to one of ordinary

skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958, F2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). To establish a *prima facie* case of obviousness, the Board must, *inter alia*, show "some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). "The motivation, suggestion or teaching may come explicitly from statements in the prior art, the knowledge of one of ordinary skill in the art, or, in some cases the nature of the problem to be solved." *Kotzab*, 217 F.3d at 1370, 55 USPQ2d at 1317. The suggestion or motivation to modify the reference does not have to be in the references themselves. See MPEP §2142. In this case, the motivation to insert the cPPT and CTS upstream and downstream the coding sequence of a transgene in a retroviral transfer vector is immediately apparent to one skilled in the art based on the teachings of the Charneau references regarding their roles in DNA synthesis. Thus, the combination of the Verma publication and the Charneau references is properly motivated.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LOUISE HUMPHREY whose telephone number is (571)272-5543. The examiner can normally be reached on Mon-Thu, 9:00 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./

Examiner, Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648